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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,563	12/10/2003	Theresa O'Keefe	10448-213001 / MPI01-244P	9540
26161 7590 04/12/2007 FISH & RICHARDSON PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER BLANCHARD, DAVID J	
			ART UNIT	PAPER NUMBER
			1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/733,563	O'KEEFE ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 January 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 9-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 9-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-8 are cancelled.
Claims 9 and 12 have been amended.
2. Claims 9-12 are pending and under consideration.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
4. This Office Action contains New Grounds of Rejections.

Withdrawn Objections/Rejections

5. The rejection of claims 9-12 under 35 U.S.C. 112, first paragraph, for lack of scope of enablement is withdrawn in view of the amendments to the claims.
6. The rejection of claims 9-12 under 35 U.S.C. 102(a) as being anticipated by Horvath et al [a] (WO 01/70266 A2, published 9/27/2001) is withdrawn in view of applicants' arguments and the Declaration under 37 CFR 1.132 of Dr. Theresa O'Keefe filed 1/10/2007.
7. The rejection of claims 9-12 under 35 U.S.C. 102(e) as being anticipated by Horvath et al [b] (US Patent 6,663,863 B2, priority at least to 3/15/2001) is withdrawn in view of applicants' arguments and the Declaration under 37 CFR 1.132 of Dr. Theresa O'Keefe filed 1/10/2007.

Response to Arguments

8. The rejection of claims 9-12 under 35 U.S.C. 103(a) as being unpatentable over LaRosa et al [a] (US Patent 6,727,349 B1, priority to 2/3/2000) in view of Bonnefoy et al (WO 99/58679, 11/18/1999) is maintained.

The response filed 1/10/2007 requests withdrawal of the rejection because the present application was subject to an obligation to assign to Millennium Pharmaceuticals, Inc. and US Patent 6,727,349 was assigned to Millennium Pharmaceuticals, Inc at the time the invention was made. This has been fully considered but is not found persuasive because being *subject to an obligation to assign*

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does not establish common ownership at the time the invention was made. It is reiterated that a statement by the attorney of record, in a clear and conspicuous manner, that: "Application X and Patent A were, at the time the invention of Application X was made, owned by Company Z." would be sufficient evidence to disqualify Patent A from being used in a rejection under 35 U.S.C. 103(a) against the claims of Application X. See MPEP 706.02(I)(2) under the heading "Evidence Required to Establish Common Ownership".

9. The rejection of claims 9-12 under 35 U.S.C. 103(a) as being unpatentable over LaRosa et al [b] (US Patent 6,696,550 B2, priority to 2/3/2000) in view of Bonnefoy et al (WO 99/58679, 11/18/1999) is maintained.

The response filed 1/10/2007 requests withdrawal of the rejection because the present application was subject to an obligation to assign to Millennium Pharmaceuticals, Inc. and US Patent 6,727,349 was assigned to Millennium Pharmaceuticals, Inc at the time of filing. This has been fully considered but is not found persuasive because being *subject to an obligation to assign* does not establish common ownership at the time the invention was made. It is reiterated that a statement by the attorney of record, in a clear and conspicuous manner, that: "Application X and Patent A were, at the time the invention of Application X was made, owned by Company Z." would be sufficient evidence to disqualify Patent A from being used in a rejection under 35 U.S.C. 103(a) against the claims of Application X. See MPEP 706.02(I)(2) under the heading "Evidence Required to Establish Common Ownership".

10. The rejection of claims 9-12 under 35 U.S.C. 103(a) as being unpatentable over Hancock et al (US 2002/0042370 A1, filed 4/13/2001, IDS reference AA filed 11/14/05) in view of Bonnefoy et al (WO 99/58679, 11/18/1999, previously cited on PTO-892 mailed 2/14/06) is maintained.

The response filed 1/10/2007 argues the specific teachings of the individual references stating that Hancock et al do not teach a preference for any particular

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isotype for the heavy chain constant region or even any particular IgG1 allotype and there is no suggestion in Hancock that the CCR2 specificity should be combined with the ability or inability to fix complement. Applicant states that the humanized antibody of Bonnefoy comprising the mutated human IgG1 constant region of SEQ ID NO:110 is a completely different humanized antibody that binds a completely different target than the claimed CCR2 humanized antibody and there is no motivation in Bonnefoy to select the specific IgG1 human heavy chain constant region of SEQ ID NO:110, nor the human kappa light chain constant region of SEQ ID NO:113 to produce the claimed humanized CCR2-specific antibodies. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In response to applicant's argument that the humanized antibody of Bonnefoy comprising the mutated human IgG1 constant region of SEQ ID NO:110 is a completely different humanized antibody that binds a completely different target than the claimed antibodies, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Hancock et al teach the claimed humanized CCR2 specific antibody and antigen-binding fragments thereof that inhibit ligand binding for treating a variety of human disorders in which activation of CCR2 is implicated and according to

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Bonnefoy, if a non-cytotoxic blocking antibody is required it is preferable to modify the generally more stable IgG1, specifically a modified human IgG1 constant region comprising two mutations (Leu²³⁵ → Ala²³⁵ and Gly²³⁷ → Ala²³⁷), identical to the claimed human IgG1 constant region of SEQ ID NO:110. Thus, while the art does recognize a subgenus of heavy chain constant region isotypes as noted by applicant, the prior art specifically teaches and suggests the desirability of using human IgG1 comprising Leu²³⁵ → Ala²³⁵ and Gly²³⁷ → Ala²³⁷ mutations (i.e., SEQ ID NO:110) as a stable non-cytotoxic blocking antibody. Therefore, one of ordinary skill in the art would have been motivated and had a reasonable expectation of success to modify the ligand blocking humanized CCR2 antibody of Hancock et al with the modified human IgG1 constant region as taught by Bonnefoy to produce a stable humanized non-cytotoxic CCR2 blocking antibody for the treatment of human disorders in which activation of CCR2 is implicated.

The Declaration of Dr. Theresa O'Keefe under 37 CFR 1.132 filed 10 January 2007 is insufficient to overcome the instant rejection because as discussed supra, the prior art of Bonnefoy et al teach the modified human IgG1 constant region of SEQ ID NO:110 and the desirability of using SEQ ID NO:110 as discussed immediately above. Further, the examiner acknowledges applicants' remarks regarding unrelated US Patent 6,682,736, however, the instant rejection is based on the combined teachings of Hancock in view of Bonnefoy et al and the relevance of US Patent 6,682,736 is not clear. Further, the existence of reference C is insufficient to support nonobviousness of cited references A and B, where C is concerned with solving a different problem of serving a different purpose than that provided in A and B.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references and the rejection is maintained.

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11. The rejection of claims 9-12 under 35 U.S.C. 103(a) as being unpatentable over LaRosa et al [c] (WO 01/57226 A1, published 8/9/2001) in view of Bonnefoy et al (WO 99/58679, 11/18/1999, previously cited on PTO-892 mailed 2/14/06) is maintained.

The response filed 1/10/2007 argues the specific teachings of the individual references stating that LaRosa et al [c] do not teach a preference for any particular isotype for the heavy chain constant region or even any particular IgG1 allotype and there is no suggestion in LaRosa et al [c] that the CCR2 specificity should be combined with the ability or inability to fix complement. Applicant states that the humanized antibody of Bonnefoy comprising the mutated human IgG1 constant region of SEQ ID NO:110 is a completely different humanized antibody that binds a completely different target than the claimed CCR2 humanized antibody and there is no motivation in Bonnefoy to select the specific IgG1 human heavy chain constant region of SEQ ID NO:110, nor the human kappa light chain constant region of SEQ ID NO:113 to produce the claimed humanized CCR2-specific antibodies. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In response to applicant's argument that the humanized antibody of Bonnefoy comprising the mutated human IgG1 constant region of SEQ ID NO:110 is a completely different humanized antibody that binds a completely different target than the claimed antibodies, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves

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or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, LaRosa et al [c] teach the claimed humanized CCR2 specific antibody and antigen-binding fragments thereof that inhibit ligand binding for treating a variety of human disorders in which activation of CCR2 is implicated and according to Bonnefoy, if a non-cytotoxic blocking antibody is required it is preferable to modify the generally more stable IgG1, specifically a modified human IgG1 constant region comprising two mutations (Leu²³⁵ → Ala²³⁵ and Gly²³⁷ → Ala²³⁷), identical to the claimed human IgG1 constant region of SEQ ID NO:110. Thus, while the art does recognize a subgenus of heavy chain constant region isotypes as noted by applicant, the prior art specifically teaches and suggests the desirability of using human IgG1 comprising Leu²³⁵ → Ala²³⁵ and Gly²³⁷ → Ala²³⁷ mutations (i.e., SEQ ID NO:110) as a stable non-cytotoxic blocking antibody. Therefore, one of ordinary skill in the art would have been motivated and had a reasonable expectation of success to modify the ligand blocking humanized CCR2 antibody of Hancock et al with the modified human IgG1 constant region as taught by Bonnefoy to produce a stable humanized non-cytotoxic CCR2 blocking antibody for the treatment of human disorders in which activation of CCR2 is implicated.

The Declaration of Dr. Theresa O'Keefe under 37 CFR 1.132 filed 10 January 2007 is insufficient to overcome the instant rejection because as discussed supra, the prior art of Bonnefoy et al teach the modified human IgG1 constant region of SEQ ID NO:110 and the desirability of using SEQ ID NO:110 as discussed immediately above.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references and the rejection is maintained.

New Grounds of Rejections

12. Claims 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horvath et al [a] (WO 01/70266 A2, published 9/27/200, cited on PTO-892 mailed 7/21/06) in view of Bonnefoy et al (WO 99/58679, 11/18/1999, previously cited on PTO-892 mailed 2/14/06).

The claims are drawn to a humanized immunoglobulin or antigen binding portion thereof having CCR2 specificity and comprising a heavy chain sequence comprising the variable heavy domain of SEQ ID NO:17 and the modified human IgG1 constant region of SEQ ID NO:110 and a light chain sequence comprising the variable light domain of SEQ ID NO:12 and the human kappa constant region (Ck) and the humanized immunoglobulin comprises two heavy chains and two light chains.

Horvath et al [a] teach a humanized CCR2 specific antibody and antigen-binding fragments thereof that inhibit ligand binding to CCR2 for treating a variety of human disorders in which activation of CCR2 is implicated, wherein the humanized antibody comprises a heavy chain sequence comprising the variable heavy domain of SEQ ID NO:17 and human IgG1 constant region and a light chain sequence comprising the variable light domain of SEQ ID NO:12 and the human kappa constant region (Ck) (see entire document, particularly pp. 17, 19-22, 25, lines 23-24 and Figs 17-18; 1D9RKA and 1D9RHA). Horvath et al [a] do not specifically teach the modified human IgG1 heavy chain constant region sequence of SEQ ID NO:110. This deficiency is made up for in the teachings of Bonnefoy et al.

Bonnefoy et al teach that if a non-cytotoxic blocking humanized antibody is required it is preferable to modify the generally more stable IgG1, specifically a modified human IgG1 constant region comprising two mutations (Leu²³⁵ → Ala²³⁵ and Gly²³⁷ → Ala²³⁷), which is identical to the claimed human IgG1 constant region of SEQ ID NO:110 (see pages 7 and 33 and Fig. 4).

It would have been *prima facie* obvious at the time of the claimed invention was made to have produced a humanized CCR2 specific antibody comprising a heavy chain comprising the variable domain of SEQ ID NO17 and the mutated human IgG1 constant

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region sequence of SEQ ID NO:110 and a light chain comprising the variable domain of SEQ ID NO:12 and the human kappa constant region of SEQ ID NO:112 and antigen-binding fragments thereof for therapeutic benefit of human disorders in which activation of CCR2 by binding of chemokines is implicated.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a humanized CCR2 specific antibody comprising a heavy chain comprising the variable domain of SEQ ID NO:17 and the mutated human IgG1 constant region sequence of SEQ ID NO:110 and a light chain comprising the variable domain of SEQ ID NO:12 and the human kappa constant region of SEQ ID NO:112 and antigen-binding fragments thereof for therapeutic benefit of human disorders in which activation of CCR2 by binding of chemokines is implicated in view of Horvath et al [a] and Bonnefoy et al because Horvath et al [a] teach a humanized CCR2 specific antibody and antigen-binding fragments thereof that inhibit ligand binding to CCR2 for treating a variety of human disorders in which activation of CCR2 is implicated, wherein the humanized antibody comprises a heavy chain sequence comprising the variable heavy domain of SEQ ID NO:17 and human IgG1 constant region and a light chain sequence comprising the variable light domain of SEQ ID NO:12 and human Ck and according to Bonnefoy et al, if a non-cytotoxic blocking humanized antibody is required it is preferable to modify the generally more stable IgG1, specifically a modified human IgG1 constant region comprising two mutations ($\text{Leu}^{235} \rightarrow \text{Ala}^{235}$ and $\text{Gly}^{237} \rightarrow \text{Ala}^{237}$), which is identical to the claimed human IgG1 constant region of SEQ ID NO:110. Therefore, one of ordinary skill in the art would have been motivated and had a reasonable expectation of success to modify the ligand blocking humanized CCR2 antibody of Horvath et al [a] with the modified human IgG1 constant region as taught by Bonnefoy et al to produce a stable non-cytotoxic humanized CCR2 blocking antibody for the treatment of human disorders in which activation of CCR2 is implicated. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been

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produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced a humanized CCR2 specific antibody comprising a heavy chain comprising the variable domain of SEQ ID NO:17 and the mutated human IgG1 constant region sequence of SEQ ID NO:110 and a light chain comprising the variable domain of SEQ ID NO:12 and the human kappa constant region of SEQ ID NO:112 and antigen-binding fragments thereof for therapeutic benefit of human disorders in which activation of CCR2 by binding of chemokines is implicated in view of Horvath et al [a] and Bonnefoy et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

13. Claims 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horvath et al [b] (US Patent 6,663,863 B2, priority at least to 3/15/2001, cited on PTO-892 mailed 7/21/06) in view of Bonnefoy et al (WO 99/58679, 11/18/1999, previously cited on PTO-892 mailed 2/14/06).

The claims have been described *supra*.

Horvath et al [b] teach a humanized CCR2 specific antibody and antigen-binding fragments thereof that inhibit ligand binding to CCR2 for treating a variety of human disorders in which activation of CCR2 is implicated, wherein the humanized antibody comprises a heavy chain sequence comprising the variable heavy domain of SEQ ID NO:17 and human IgG1 constant region and a light chain sequence comprising the variable light domain of SEQ ID NO:12 and the human kappa constant region (Ck) (see entire document, particularly col. 11-14, 16,27-29 and Figs 17-18; 1D9RKA and 1D9RHA). Horvath et al [b] do not specifically teach the modified human IgG1 heavy chain constant region sequence of SEQ ID NO:110. This deficiency is made up for in the teachings of Bonnefoy et al.

Bonnefoy et al have been described *supra*.

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It would have been *prima facie* obvious at the time of the claimed invention was made to have produced a humanized CCR2 specific antibody comprising a heavy chain comprising the variable domain of SEQ ID NO:17 and the mutated human IgG1 constant region sequence of SEQ ID NO:110 and a light chain comprising the variable domain of SEQ ID NO:12 and the human kappa constant region of SEQ ID NO:112 and antigen-binding fragments thereof for therapeutic benefit of human disorders in which activation of CCR2 by binding of chemokines is implicated.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a humanized CCR2 specific antibody comprising a heavy chain comprising the variable domain of SEQ ID NO:17 and the mutated human IgG1 constant region sequence of SEQ ID NO:110 and a light chain comprising the variable domain of SEQ ID NO:12 and the human kappa constant region of SEQ ID NO:112 and antigen-binding fragments thereof for therapeutic benefit of human disorders in which activation of CCR2 by binding of chemokines is implicated in view of Horvath et al [b] and Bonnefoy et al because Horvath et al [b] teach a humanized CCR2 specific antibody and antigen-binding fragments thereof that inhibit ligand binding to CCR2 for treating a variety of human disorders in which activation of CCR2 is implicated, wherein the humanized antibody comprises a heavy chain sequence comprising the variable heavy domain of SEQ ID NO:17 and human IgG1 constant region and a light chain sequence comprising the variable light domain of SEQ ID NO:12 and human Ck and according to Bonnefoy et al, if a non-cytotoxic blocking humanized antibody is required it is preferable to modify the generally more stable IgG1, specifically a modified human IgG1 constant region comprising two mutations (Leu²³⁵ → Ala²³⁵ and Gly²³⁷ → Ala²³⁷), which is identical to the claimed human IgG1 constant region of SEQ ID NO:110. Therefore, one of ordinary skill in the art would have been motivated and had a reasonable expectation of success to modify the ligand blocking humanized CCR2 antibody of Horvath et al [b] with the modified human IgG1 constant region as taught by Bonnefoy et al to produce a stable non-cytotoxic humanized CCR2 blocking antibody for the treatment of human disorders in which activation of CCR2 is implicated. The strongest rationale for combining

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references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced a humanized CCR2 specific antibody comprising a heavy chain comprising the variable domain of SEQ ID NO:17 and the mutated human IgG1 constant region sequence of SEQ ID NO:110 and a light chain comprising the variable domain of SEQ ID NO:12 and the human kappa constant region of SEQ ID NO:112 and antigen-binding fragments thereof for therapeutic benefit of human disorders in which activation of CCR2 by binding of chemokines is implicated in view of Horvath et al [b] and Bonnefoy et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

14. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you

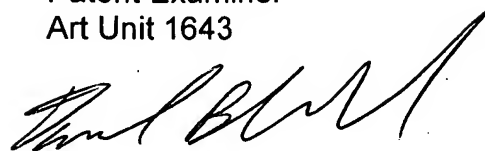
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have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J. Blanchard
Patent Examiner
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A handwritten signature in black ink, appearing to read "David J. Blanchard", written in a cursive style.

DB
April 3, 2007